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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/848,600	05/03/2001	Peter Watts	WC 111	9982

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EXAMINER	
GAMBEL, PHILLIP	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 05/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/848,600	WATTS ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114.
Applicant's submission, filed on 2/9/04, has been entered.

Applicant's amendment, filed 2/9/04, has been entered.
Claims 1-19 have been canceled.
Claims 21-35 have been added.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Action will be in response to applicant's arguments, filed 2/9/04.
The rejections of record can be found in the previous Office Actions.

3. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 C.F.R. § 1.75(d)(1) and M.P.E.P. § 608.01(l). Correction of the following is required:

Applicant is requested to identify the written support for claims "plurality of microspheres" in the specification as filed.

In the absence of written support in the specification as filed, applicant is required to amend the specification accordingly.

5. Claims 21-35 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. The specification as originally filed does not provide support for the invention as now claimed:

While the instant specification appears to provide written support for the concentrations of ICAM-1 set forth in claims 22, 23, 29, 30 and 36 with respect to chitosan (e.g. see page 4, paragraph 4 of the instant specification), the specification as filed does not appear to provide sufficient written description for such ICAM-1 concentrations in the context of the other bioadhesive materials.

In addition, while the specification as filed does provide written support for "0.1% to 50%" ICAM-1 in gelatin microspheres (see page 8, paragraph 4), the specification as filed does not appear to provide sufficient written description for "about 0.1% to 50%" nor for the "0.1% to 50%" in the context of bioadhesive materials other than gelatin.

Applicant's reliance on generic disclosure and possibly a single or limited species do/does not provide sufficient direction and guidance to the "features" currently claimed. It is noted that a generic or a sub-generic disclosure cannot support a species unless the species is specifically described. It cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads. See In re Smith 173 USPQ 679, 683 (CCPA 1972) and MPEP 2163.05.

Furthermore, the disclosure of the chemical or physical bonds recited in claim 28 as well as the "which composition adheres to the epithelia and/or mucosal surface of the nasal cavity upon administration" in the specification as filed. Therefore, these claimed limitations are considered new matter, unless applicant can provide sufficient written description in the specification as filed.

Applicant's amendment, filed 2//9/04 directs support to pages 4 and 8 of the specification as well as the original claims for the written description for the above-mentioned "limitations".

However, the specification as filed does not provide a written description or set forth the metes and bounds of this phrase. The specification does not provide sufficient blazemarks nor direction for the instant products and methods encompassing the above-mentioned "limitations" as currently recited. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office action

Alternatively, applicant is invited to provide sufficient written support for the "limitations" indicated above. See MPEP 714.02 and 2163.06

6. Claim 22 is objected to because there should be a comma (,) between "starch" and "chitosan" and the term "gellan" is recited twice in the same Markush recitation.

Claim 35 is objected to because it should be "Van der Waals" and not "Van de Waals".

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 21-35 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Igari et al. (U.S. Patent NO. 5,482,706; 1449) AND/OR Greve et al. (U.S. Patent No. 5,589,453; 1449) in view of Wegner et al. (U.S. Patent No. 5,7300,983; 1449), Gwaltney et al. (U.S. Patent N. 5,422,097; 1449), Illum (U.S. Patent No. 5,690,954; 1449), Illum (U.S. Patent No. 5,707,644; 1449) andKublik et al. (Eur. J. Pharm. Biopharm. 39: 192-196, 1993 ; 1449) essentially for the reasons of record.

Applicant's arguments, filed 2/9/04, have been fully considered but are not found convincing essentially for the reasons of record.

Applicant's arguments and the examiner's rebuttal are essentially the same of record.

Again, applicant acknowledged that Greve teaches a water soluble preparation of human rhinovirus major receptors that reduce viral infectivity, but then argues that Greve does not teach that the preparation can be formulated into any type of pharmaceutical compositions, nor demonstrate any in vivo use of the preparation.

In contrast to applicant's assertions that Greve is a basic science reference, applicant is reminded that the claims of Greve encompass methods of reducing infection by human rhinovirus with human rhinovirus receptor protein (i.e. ICAM-1) and that U.S. patents are presumed valid (see 35 USC 282).

Again, applicant argues that Wegner is designed for systemic delivery of ICAM-1 to lung endothelia and not to the nasal cavity and does not teach the use of ICAM-1 with microspheres formulated from chitosan, gelatin, hyaluronic acids, alginate and gellan.

Again, applicant acknowledges that Gwaltney teaches compositions which prevent the attachment of rhinovirus to nasal cells, including ICAM-1, but argues that Gwaltney does not teach the use of microspheres and liquid formulations comprising chitosan.

Again, acknowledges that Illum '954 and Illum '644 teach drug delivery compositions comprising starch, gelatin, dextran, collagen and gellan but these references do not teach compositions comprising ICAM-1.

Applicant acknowledges that Kublik teach drug compositions for nasal applications comprising gellan and hydroxymethylcellulose but does not each chitosan nor ICAM-1.

Applicant asserts that the present invention addressing the difficulty in administering an active agent to the nasal cavity.

Applicant asserts that the combination of the references do not teach nor suggest each element of the claimed invention, including (1) a composition that includes chitosan and ICAM-1, (2) a composition that includes a plurality of microspheres aof the recited materials and ICAM-1, (3) an ICAM-1 composition that is adapted to be adhered to the epithelia and/or mucosal surface of the nasal cavity, (4) a method of treating a viral infection affecting the nasal cavity including adhering an antivirally effective amount of the recited composition to the epithelia and/or mucosal surface of the nasal cavity, (5) a method of using ICAM-1 composition that includes the recited bioadhesives and (6) a method of improving the retention of an ICAM-1 composition in the nasal cavity.

Again as pointed out previously, once a prima facie case of obviousness has been made the burden of going further is shifted to applicant. In re Keller, 642 F.2d 4B, 208 USPQ 871, 882 (CCPA 1981). This applicant has not done, but rather argues the references individually and not their combination. One cannot show non-obviousness by attacking references individually where the rejections are based on a combination of references. In re Young 403 F.2d 759, 150 USPQ 725 (CCPA 1968). See MPEP 2145.

In response to applicant's arguments that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fine 5 USPQ2d 1596 (Fed. Cir 1988) and In re Jones 21 USPQ2d 1941 (Fed. Cir. 1992).

In this case the teachings of the references are clearly drawn to providing the HRV receptor or ICAM-1 to inhibit rhinovirus attachment and infectivity, including providing ICAM-1 to those areas susceptible to infection by rhinovirus (e.g. see Igari and Greve).

In addition, all of the references provide for appropriate pharmaceutical compositions comprising an active ingredient and

teach the delivery of compositions comprising ICAM-1 (e.g. column 5, line 4), chitosan, gelatin, microspheres, polymeric materials for nasal delivery (e.g. see Igari, see entire document, including Abstract, Summary of the Invention, Description of the Preferred Embodiments, columns 7-12, particularly column 9-10);

teach the use of HRV receptor or ICAM-1 to inhibit rhinovirus attachment and infectivity, including providing ICAM-1 to those areas susceptible to infection by rhinovirus such as intranasal sprays (e.g. see Greve, seen entire document, including Summary of the Invention, Description of the Preferred Embodiments, column 4, paragraph 2);

teach delivering ICAM-1 derived antagonists, including controlled releas preparations and polymeric materials (see Wegner, see entire document, including Detailed Description of the Preferred Embodiments, including Administration or the Compositions of the Present Invention on columns 15-16);

teach the use of antiviral ICAM-1 (column 10), including preparation of such antiviral agents for intranasal delivery (e.g. see Gwaltney, see entire document, particularly Description of the Preferred Embodiments, including columns 11-12, overlapping paragraph); and

teach various bioadhesive formulations encompassed by the claimed invention for drug delivery to the nasal cavity, as well as the various considerations of mixing said bioadhesives materials with a wide variety of active drugs to increase bioavailability upon administration (See entire documents of Illum '954, Illum '644 and Kublik et al.).

Furthermore as an example, Illum '954 teaches that the bioadhesive formulations and delivery systems provide for great bioavailability of the active drug and that certain formulations are due to the greater retention of the delivery systems in the nasal cavity (e.g. see column 4, paragraph 1-4, column 6, paragraph 2; column 8, paragraphs 5-6). Also, Illum '954 teaches various Examples of concentrations, including 0.5, 2, 4, and 5% w/v Rose Bengal (see columns 7-8, overlapping paragraph).

In addition, as pointed out previously, Illum '644 teaches that the amount of the drug that can be carried by the microspheres is termed the loading capacity, which is determined by the physico-chemical properties of the drug molecules and, in particular its size and affinity for the particle matrix (see column 6,paragraph 3). It was known that for many peptides and proteins the amount of drug substances to be administered for a resultant therapeutic effect would be on the order of a few micrograms or less.

Given the teachings of the prior art, including the motivation and expectation of success in providing an antiviral effective amounts of ICAM-1 to the nasal cavity; it would have been obvious and expected that the various w/v concentrations encompassed by the claims would have been provided in inhibiting rhinovirus attachment and infectivity based on the needs of the patient sand the nature of the viral infection by the ordinary artisan at the time the invention was made. The prior art teaches the various bioadhesive materials encompassed by the claimed invention for the purposes of increasing the bioavailability of active substances. Also, Illum '9564 teach an example of various concentrations of an active substance in polymeric bioadhesive materials that read on the claimed limitations, providing evidence that various concentrations of active ingredients would have been expected at the time the invention was made.

Also, it is noted that where the general condition of a claim is disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation see In re Aller, 105 USPQ 233, 235 (CCPA 1955). See MPEP 2144.05.

Further a particular parameter must first be recognized as a result-effective variable, a variable which achieves a recognized results, before the determination of the optimum or workable ranges of said variable might characterized as routine experimentation. See In re Antoine, 195 USPQ 6 (CCPA 1977). See MPEP 2144.05.

The prior art clearly provided sufficient motivation and expectation of success of administering an antiviral effective amount of ICAM-1 to the nasal cavity to treat rhinovirus infections and combining ICAM-1 with formulations comprising microspheres and/or the claimed bioadhesives would have been expected and desired formulations to provide antiviral agents such as ICAM-1 to the nasal cavity at the time the invention was made by the ordinary artisan. The strongest rationale for combining references is a recognition, expressly or implicitly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent that some advantage or expected beneficial result would have been produced by their combination. See In re Sernaker 17 USPQ 1, 5-6 (Fed. Cir. 1983). See MPEP 2144.

Here, the prior art teaches providing ICAM-1 to combat rhinovirus infection, including intranasal administration and the use of polymeric compositions. In addition, the prior art teaches the various bioadhesive materials encompassed by the claimed invention, including their use with a variety of active drugs to achieve increase bioavailability of said active drugs. As pointed herein and previously, Illum'644 teaches that the amount of the drug that can be carried by the microspheres is termed the loading capacity which is determined by the physico-chemical properties of the drug molecules and in particular its size and affinity for the particle matrix (see column 6, paragraph 32). The claimed limitations of the compositions formulated to comprise ICAM-1 with bioadhesive materials were well within the purview, motivation and expectation of success of the ordinary artisan at the time the invention was made to provide an increased bioavailability of an antiviral effective amount of ICAM-1 intranasally.

Although applicant asserts that the prior art do not each the adherence of ICAM-1 compositions to the epithelia and/or mucosal surface of the nasal cavity, the prior art clearly provides for administering an effective amount of ICAM-1 to treat viral infections and the use of bioadhesives to increase bioavailability of pharmaceutical agents. Therefore, it would have been readily appreciated by the ordinary artisan at the time the invention was made that ICAM-1 bioadhesive compositions would adhere to epithelial and mucosal surfaces. Similarly, the ordinary artisan would have administered a plurality of microspheres and not a single microsphere to achieve a therapeutic antiviral effect. Furthermore, it would have been expected or intrinsic to ICAM-1 bioadhesive compositions to encompass adherence by well known chemical or physical bonds of molecular interactions.

One of ordinary skill in the art at the time the invention was made would have been motivated to provide ICAM-1 with a bioadhesive, including those encompassed by the claimed invention to increase the bioavailaibility with a bioadhesive, including those encompassed by the claimed invention to increase the bioavailability of ICAM-1 in order to inhibit rhinovirus attachment and infectivity. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments are not found persuasive.

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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May 17, 2004